

AppIn. No. 09/890,3/1
Amendment dated May 10, 2009
Reply to Office Action dated December 11, 2008

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-53. (Canceled)

Claim 54. (Previously presented) A method for administering a pharmaceutical composition to a patient in need thereof, comprising:

transnasally administering to the patient a pharmaceutical composition, the pharmaceutical composition comprising:

an active ingredient; and

a carrier comprising a penetrant suspended or dispersed in a solvent,

the penetrant comprising a minute fluid droplet surrounded by a coating of at least one layer of at least two substances, the substances differing by at least a factor of 10 in solubility in a liquid medium,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least two substances, the average diameter of homoaggregates of the more soluble substance or the average diameter of the heteroaggregates of the at least two substances being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance is up to 99 mol-% of the concentration required to solubilize the droplet or corresponds to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least five times lower than the deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains

and wherein the less soluble substance is a lipid and the more soluble substance is a surfactant or more soluble form of the lipid.

Claim 55. (Previously presented) The method of claim 54, wherein the at least two substances are two forms of a substance.

Claim 56. (Previously presented) The method of claim 54, wherein the active ingredient is an allergen.

Claim 57. (Previously presented) The method of claim 54, wherein the active ingredient is an antigen.

Appl. No. 09/890,371
Amendment dated May 10, 2009
Reply to Office Action dated December 11, 2008

Claim 58. (Previously presented) The method of claim 54, further comprising a compound that is a cytokine or a compound that induces cytokine or anti-cytokine activity.

Claim 59. (Previously presented) The method of claim 58 wherein the cytokine is IL-4, IL-3, IL-2, TGF, IL-6, TNF, IL-1 α , IL-1 β , a type I interferon, IFN- α , IFN β , IL-12, IFN- γ , TNF- β , IL-5 or IL-10.

Claim 60. (Previously presented) The method of claim 58 wherein the compound with anti-cytokine activity is an anti-cytokine antibody or active fragment thereof.

Claim 61. (Previously presented) The method of claim 58 wherein the compound that is a cytokine or induces cytokine or anti-cytokine activity and the active ingredient are associated with the penetrant.

Claim 62. (Previously presented) The method of claim 54, wherein the less soluble substance is a lipid, and the more soluble substance is a surfactant.

Claim 63. (Previously presented) The method of claim 54, wherein the less soluble substance is a lipid, and the more soluble substance is a more soluble form of the lipid.

Claim 64. (Canceled)

Claim 65. (Previously presented) The method of claim 54, wherein the more soluble substance solubilizes the penetrating droplet and is present in concentration not exceeding 99 mol% of the concentration required to disintegrate the droplet or not exceeding 99 mol% of the saturating concentration in the unsolubilized droplet, whichever is higher.

Claim 66. (Previously presented) The method of claim 54, wherein the less soluble substance is a polar lipid and the more soluble substance is a surfactant.

Claim 67. (Previously presented) The method of claim 54, wherein the less soluble substance is a polar lipid and the more soluble substance is a polar lipid.

Claim 68. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 25 nm and 500 nm.

Claim 69. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 30 nm and 250 nm.

Claim 70. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 35 nm and 200 nm.

Claim 71. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 40 nm and 150 nm.

Claim 72. (Previously presented) The method of claim 54, wherein the concentration of penetrant is 0.001 to 20 weight-% of total dry mass in the pharmaceutical composition.

Appln. No. 09/890,371
Amendment dated May 10, 2009
Reply to Office Action dated December 11, 2008

Claim 73. (Previously presented) The method of claim 54, wherein the concentration of penetrant is between 0.01 w-% and 15 w-% of total dry mass in the pharmaceutical composition.

Claim 74. (Previously presented) The method of claim 54, wherein the concentration of penetrant is between 0.1 w-% and 12.5 w-% of total dry mass in the pharmaceutical composition.

Claim 75. (Previously presented) The method of claim 54, wherein the concentration of penetrant is between 0.5 w-% and 10 w-% of total dry mass in the pharmaceutical composition.

Claim 76. (Previously presented) The method of claim 54, wherein the liquid medium is a supporting medium.

Claim 77. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 1 mM and 500 mM.

Claim 78. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 10 mM and 400 mM.

Claim 79. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 50 mM and 300 mM.

Claim 80. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 100 mM and 200 mM.

Claim 81. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution.

Claim 82. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible buffer with pH of between 4 and 10.

Claim 83. (Previously presented) The method of claim 54, wherein the active ingredient concentration is between 0.001 and 40 weight-% of total penetrant mass.

Claim 84. (Previously presented) The method of claim 54, wherein the active ingredient concentration is between 0.01 w-% and 30 w-% of total penetrant mass.

Claim 85. (Previously presented) The method of claim 54, wherein the active ingredient concentration is between 0.1 w-% and 25 w-% of total penetrant mass.

Claim 86. (Previously presented) The method of claim 54, wherein the active ingredient concentration is between 0.5 w-% and 15 w-% of total penetrant mass.

Appl. No. 09/890,371
Amendment dated May 10, 2009
Reply to Office Action dated December 11, 2008

Claim 87. (Previously presented) The method of claim 54, wherein the applied penetrant dose is between 0.01 mg and 15 mg per nostril.

Claim 88. (Currently amended) The method of claim 54, wherein the pharmaceutical composition formulation is administered using a metered delivery device.

Claim 89. (Currently amended) The method of claim 54, wherein the penetrants are in suspension and further comprising loading the penetrants with the active ingredient within 24 hours prior to the formulation administration before transnasal administration.

Claim 90. (Previously presented) The method of claim 54, wherein a target site of the active ingredient is a nervous system.

Claim 91. (Previously presented) The method of claim 90 wherein the target site is a brain.

Claim 92. (Previously presented) The method of claim 54, wherein the pharmaceutical composition is a vaccine.

Claim 93. (Previously presented) The method of claim 92, wherein the vaccine further comprises a pathogen extract or a compound from a pathogen or a fragment or a derivative thereof.

Claim 94. (Previously presented) The method of claim 92, wherein the vaccine further comprises an adjuvant.

Claim 95. (Previously presented) The method of claim 94, wherein the adjuvant is lipopolysaccharide, or an extract of a microorganism.

Claim 96. (Previously presented) The method of claim 92, wherein the vaccine comprises MPL and IL-12 or GM-CSF and IL-4.

Claim 97. (Previously presented) The method of claim 92, wherein at least two doses of vaccine are administered.

Claim 98. (Previously presented) The method of claim 92, wherein the vaccine is administered as a booster vaccination.

Claim 99. (Previously presented) The method of claim 92, wherein the time interval between the subsequent vaccinations is between 2 weeks and 5 years.

Claim 100. (Previously presented) A method for administering a pharmaceutical composition to a patient in need thereof, comprising:

transnasally administering to the patient a pharmaceutical composition,

Appln. No. 09/890,371
Amendment dated May 10, 2009
Reply to Office Action dated December 11, 2008

wherein the pharmaceutical composition is for the treatment of infective diseases, endocrine disorders, adrenal disorders, gastrointestinal disorders, hemorrhagic diseases, musculoskeletal and connective tissue disorders, neurological disorders, oncological disorders, psychiatric disorders, and/or for use in the field of gynecology, and/or for use in the field of immunology,

the pharmaceutical composition comprising:

an active ingredient; and

a carrier comprising a penetrant suspended or dispersed in a solvent,

the penetrant comprising a minute fluid droplet surrounded by a coating of at least one layer of at least two substances, the substances differing by at least a factor of 10 in solubility in a liquid medium,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least two substances, the average diameter of homoaggregates of the more soluble substance or the average diameter of the heteroaggregates of the at least two substances being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance is up to 99 mol-% of the concentration required to solubilize the droplet or corresponds to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least five times lower than the deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains

and wherein the less soluble substance is a lipid and the more soluble substance is a surfactant or more soluble form of the lipid.

Claim 101. (Previously presented) The method of claim 100, wherein the active ingredient is an antigen.

Claim 102. (Previously presented) The method of claim 101, wherein the antigen is derived from a pathogen.

Claim 103. (Previously presented) The method of claim 100, wherein the active ingredient is an allergen.

Claim 104. (Canceled).

Claim 105. (New) The method of claim 54, wherein the active ingredient comprises at least one of the group consisting of a peptide, a peptide derivative, a polypeptide, a polypeptide derivative, a protein, and a protein derivative.

Appln. No. 09/890,371

Amendment dated May 10, 2009

Reply to Office Action dated December 11, 2008

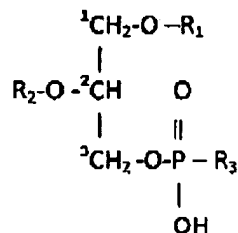
Claim 106. (New) The method of claim 54, wherein the active ingredient is a polypeptide or a protein.

Claim 107. (New) The method of claim 54, wherein the active ingredient comprises at least one of the group consisting of insulin, IFN-gamma, Tetanus toxoid, GM-CSF, IL-4, IL-12, monophosphoryl lipid A, Cholera toxin, and Heat Labile toxin.

Claim 108. (New) The method of claim 54, wherein the active ingredient is an immunologically active substance.

Claim 109. (New) The method of claim 54, wherein the less soluble substance comprises a phospholipid.

Claim 110. (New) The method of claim 109, wherein the phospholipid has the chemical formula:



where R_1 and R_2 is a C_{10-20} -acyl or -alkyl or a partly unsaturated fatty acid residue, and where R_3 is hydrogen, 2-trimethylamino-1-ethyl, 2-amino-1-ethyl, C_{1-4} -alkyl, C_{1-5} -alkyl substituted with carboxy, C_{2-5} -alkyl substituted with hydroxy, C_{2-5} -alkyl substituted with carboxy and hydroxy, or C_{2-5} -alkyl substituted with carboxy and amino, inositol, sphingosine, or salts of said substances.

Claim 111. (New) The method of claim 110, wherein the unsaturated fatty acid residue is an oleoyl-, palmitoleoyl-, elaidoyl-, linoleyl-, linolenyl-, linolenoyl-, arachidoyl-, vaccinylyl-, lauroyl-, myristoyl-, palmitoyl-, or stearoyl chain.

Claim 112. (New) The method of claim 109, wherein the lipid is at least one of the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, phosphatidylinositol, phosphatidic acid, phosphatidylserine, and sphingophospholipid.

Claim 113. (New) The method of claim 54, wherein the lipid comprises soybean phosphatidylcholine.

Claim 114. (New) The method of claim 54, wherein the less soluble substance is soybean phosphatidylcholine; the more soluble substance is Tween-80, sodium cholate or cholic acid; and the active ingredient is a peptide or protein.